UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Revised Nabam Mutagenicity Studies

TO: David Giamporcaro
SPRD

FROM: Byron T. Backus
Toxicology Branch
HED (TS-769C)

THROUGH: Marcia van Gemert, Ph.D., Section Head
Review Section III
Toxicology Branch
HED (TS-769C)

Judith W. Hauswirth, Ph.D., Toxicologist
Toxicology Branch
Hazard Evaluation Divison (TS-769C)

Ted Farber, Ph.D., Chief
Toxicology Branch
Hazard Evaluation Division (TS-769C)

Compound: Nabam

Caswell #585 Tox. Project No. 2044

Background:

Two mutagenicity studies on the subject chemical have been revised and resubmitted. The original submissions were reviewed some time ago (B. Backus, 05/15/86, Coberly file no. 005114).

Comments and Recommendations:

1. The revised report in Acc. 263346 titled "Clastogenic evaluation of Nabam 30% water solution, Alco/Vining/Uniroyal, lot no. 281770P in the rat bone marrow cytogenetics assay" (conducted by Litton Bionetics) has been examined. The only revision noted was that "some of the animals which were dosed with the test article were outside of the ±15% mean weight limits as stated by the protocol."

This revision does not affect the previous review comments and/or conclusions made regarding this study.

It is noteworthy that the revised report still includes the statement on p. 3: "Additional information supplied by the client included an acute oral toxicity level in rats of 810 mg/kg, and an LD_{50} of 500 mg/kg." As previously noted, if the information received from the sponsor was that the oral toxicity was 810 mg/kg and the LD_{50} was 500 mg/kg (sex not specified), either the values were transposed, or one is in error since toxicity generally occurs at levels below the LD_{50} value rather than above it."

2. In the revised report (Acc. 263347) titled "Clastogenic evaluation of Nabam, 30% water solution, Alco/Vining/Uniroyal, lot #28177DP, an in vitro cytogenetic assay measuring sister chromatid exchange in Chinese hamster ovary (CHO) cells" there have been a number of minor corrections and revisions.

In the original review (B. Backus, 05/15/86, Coberly file no. 005114) in the section containing reviewer's discussion and interpretation of study results (see p. 11 of Dynamac Review 1-019F, dated April 10, 1986) it was noted that:

> In the nonactivated assay...the average percent of M_1 cells ranged from 53.5 (1000 ug/mL) to 88.5% (5000 ug/mL), demonstrating a slight to marked mitotic cell cycle delay and, as a consequence, a depression of second division metaphases (M_2 cells) at all doses...(This) was sufficient evidence to warrant a repeat study with an extended expression period...

Mitotic delay was also observed in the S9-activated assays.

Revisions to the the amended final report (see p. iv of the submitted material) include the following which are relevant to cell cycle delay:

> Page 5 Section IX. 1. Line 13 - Sentence changed to read "Excessive cell cycle delay was not noted..."
>
> Page 7 Section X.C. Line 22 through 23 - Sentence added "Cell cycle delay was observed in all cultures which were evaluated for SCE.

It is concluded that these changes, as well as the others made in the revised report in Acc. 263347, are such that no ~~any~~ revision(s) are necessary in the original Toxicology Branch review.